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4/30/87

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: David B. Anderson, et al. )  
Serial No.: 811,059 )  
Filed : December 19, 1985 ) Group Art Unit: 125  
For : GROWTH PROMOTION ) Examiner: F. Waddell  
Docket No.: X-5683B )

PETITION TO CORRECT INVENTORSHIP UNDER 37 C.F.R. 1.48

Commissioner of Patents and Trademarks  
Washington, D.C. 20231

Sir:

Applicants of the above-captioned application <sup>GROUP 125</sup> hereby petition and request the Commissioner to correct the inventorship in the subject application by joining as coinventor Ronald R. Tuttle.

The accompanying papers include a Declaration under 37 C.F.R. 1.63, a Declaration by Applicants Anderson, Schmiegel, and Veenhuizen under 37 C.F.R. 1.48, a written consent of the assignee, Eli Lilly and Company, and an authorization to charge assignee's account in the amount of the petition fee set forth in 37 C.F.R. 1.7(h).

The claims as originally presented and allowed in the above-captioned application were directed to a method of promoting growth and improving feed efficiency in ruminants by administering a compound known within Eli Lilly and Company as 31537. Claims were also presented to a method for improving leanness in domesticated animals comprising administering 31537. Compound 31537 is a 3-phenyl-4-aminobenzamide having two asymmetric carbon atoms, and accordingly exists as four distinct optical isomers. Applicants very recently established that most

of the activity exhibited by 31537 appears to be attributable to one of the four individual isomers, namely a compound known within Eli Lilly and Company as compound 99134. The data establishing 99134 as the most potent component of compound 31537 was submitted to the Office by a paper dated January 22, 1987. That same paper offered amendments to the claims whereby the use of the specific optical isomer 99134 for improving feed efficiency and promoting growth in ruminants and improving leanness in domesticated animals were added. By way of a telephone conversation on February 25, 1987, the Examiner advised Applicants' attorney that the proposed amendments would be entered and that all claims would be allowed. Upon reviewing the background record upon which the above-captioned application is based, Applicants' attorney believes that Dr. Ronald R. Tuttle made an inventive contribution to the invention embraced specifically by newly added Claim 42, which is directed to a method of improving leanness in domesticated animals comprising administering 99134.

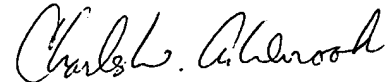
The accompanying Declaration by Anderson, Schmiegel, and Veenhuizen establishes that both Schmiegel and Veenhuizen had conversations with Dr. Tuttle concerning the use of 99134 for improving leanness in dogs prior to the time when Schmiegel, Veenhuizen, and Anderson conceived and reduced to practice the invention of promoting growth and improving feed efficiency in ruminants with 31537 and improving leanness in domesticated animals with 31537. The omission of Dr. Tuttle as an inventor on the application as originally filed occurred without any deceptive intention on the part of the Applicants actually recited at the time of filing. Moreover, the contribution made

by Dr. Tuttle concerning the use of 99134 was not earlier brought to the attention of the Office because the effectiveness of 99134 was only recently confirmed as described in detail by the Declaration of Dr. Anderson already of record.

As pointed out in more detail in the accompanying Declaration by Anderson, Schmiegel, and Veenhuizen, Dr. Schmiegel and Mr. Veenhuizen both had discussions with Dr. Tuttle sometime around the beginning of 1979 which demonstrated that Dr. Tuttle had investigated 99134 and had concluded that it was effective for improving lean mass in dogs. While Dr. Tuttle did not make a suggestion concerning growth promotion and feed efficiency improvement employing 99134 or any other phenethanolamine, nor did he suggest the use of 31537 for improving leanness in animals, it was the discussions with Dr. Tuttle that prompted Mr. Veenhuizen and Dr. Schmiegel to pursue the development of phenethanolamines and to investigate a number of such compounds as potential growth promoters and improvers of feed efficiency and leanness. Applicants have established by voluminous data already presented in this case, and in the parent cases, that 31537, and now 99134, appear to have unexpectedly superior growth promotion properties, and the ability to improve feed efficiency and leanness, relative to other  $\beta$ -phenethanolamines of the same general structural class.

In view of the foregoing comments and the accompanying declaration and other documents, Applicants respectfully request the Commissioner to grant this Petition to correct the inventorship and to add Dr. Ronald R. Tuttle as a coinventor in the above-captioned application.

Respectfully submitted,



Charles W. Ashbrook  
Attorney for Applicants  
Registration No. 27,610

Phone: 317-276-6015

Eli Lilly and Company  
Patent Division/CWA  
Lilly Corporate Center  
Indianapolis, Indiana 46285

March 23, 1987



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BAPC  
W41

# FEE AUTHORIZATION LETTER

ATTORNEY'S DOCKET NO.

X-5683B

SERIAL NO.

811,059

FILING DATE

12/19/85

EXAMINER

F. Waddell

GROUP ART UNIT

125

IN RE APPLICATION OF

David B. Anderson, et al.

For: GROWTH PROMOTION

## TO THE COMMISSIONER OF PATENTS AND TRADEMARKS:

- ☐ Applicant(s) petition(s) for an extension of time under 37 C.F.R. 1.136 to file the accompanying:
- ☐ Response within one month of original due date (\$56.00)
  - ☐ Response within two months of original due date (\$170.00)
  - ☐ Response within three months of original due date (\$390.00)
  - ☐ Response within four months of original due date (\$610.00)

☐ The accompanying papers include amended claims. The fee has been calculated as follows:

### CLAIMS AS AMENDED

(1)	(2) CLAIMS REMAINING AFTER AMENDMENT	(3)	(4) HIGHEST NUMBER PREVIOUSLY PAID FOR	(5) NO. OF EXTRA CLAIMS PRESENT	(6) RATE	(7) ADDITIONAL FEE
TOTAL CLAIMS	*	MINUS	**	=	× \$12	=
INDEP. CLAIMS	*	MINUS	***	=	× \$34	=
TOTAL ADDITIONAL FEE FOR THIS AMENDMENT						

\*If the entry in column 2 is less than the entry in column 4, write "0" in column 5.

\*\*If the "Highest Number Previously Paid For" IN THIS SPACE is less than 20, write "20" in this space.

\*\*\*If the "Highest Number Previously Paid For" IN THIS SPACE is less than 3, write "3" in this space.

☒ The following other fees are incurred by the accompanying papers.

- ☒ Petition to Correct Inventorship
- ☐ Under 37 C.F.R. 1.48 (\$140.00)

Please charge DEPOSIT ACCOUNT NO. 05-0830 in the amount of \$140.00

Two copies of this sheet are enclosed.

*Charles W. Ashbrook*

Charles W. Ashbrook  
Attorney for Applicants  
Registration No. 27,610

Phone: 317-276-6015

Eli Lilly and Company  
Patent Division/CWA  
LILLY CORPORATE CENTER  
Indianapolis, Indiana 46285

*March 23, 1987*

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25  
1987

#17  
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4/30/87  
RECEIVED

APR 10 1987

GROUP 120

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: David B. Anderson, et al. )  
Serial No.: 811,059 )  
Filed : December 19, 1985 ) Group Art Unit: 125  
For : GROWTH PROMOTION ) Examiner: F. Waddell  
Docket No.: X-5683B )

CONSENT BY ASSIGNEE UNDER 37 C.F.R. 1.48

Commissioner of Patents and Trademarks

Washington, D.C. 20231

Sir:

Eli Lilly and Company, a corporation of Indiana, as assignee of the entire right, title and interest in and to the above-identified patent application by virtue of the assignments of coinventors, David B. Anderson, Klaus K. Schmiegel, Edward L. Veenhuizen, and Ronald R. Tuttle, copies of which are attached hereto, hereby consents to the joining of Ronald R. Tuttle as coinventor of the invention claimed in the above-captioned application as sought in the accompanying Petition to Correct Inventorship.

Respectfully,

ELI LILLY AND COMPANY

*E. B. Herr, Jr.*  
E. B. Herr, Jr.  
Executive Vice President

ATTEST:

*For Secretary*  
Assistant Secretary

*March 18 1987*  
Date

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APR 10 1987

GROUP 120

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: David B. Anderson, et al. )  
Serial No.: 811,059 )  
Filed : December 19, 1985 ) Group Art Unit: 125  
For : GROWTH PROMOTION ) Examiner: F. Waddell  
Docket No.: X-5683B )

DECLARATION BY DAVID B. ANDERSON, KLAUS K. SCHMIEGEL,  
AND EDWARD L. VEENHUIZEN UNDER 37 C.F.R. 1.48

Commissioner of Patents and Trademarks

Washington, D.C. 20231

Sir:

We, David B. Anderson, Klaus K. Schmiegel, and Edward L. Veenhuizen hereby declare and say as follows:

We are the same parties named as coinventors in the above-captioned application. At the time we signed the Declaration in the above-captioned application, we were of the belief that we were the sole inventors of the subject matter disclosed and claimed therein. We were not at that time claiming a method for improving leanness in animals employing the specific compound known within Eli Lilly and Company as 99134. We have now learned that the observation that 99134 was effective in increasing leanness in dogs was made by Dr. Ronald R. Tuttle, our former associate at Eli Lilly and Company.

Two of us, Dr. Schmiegel and Mr. Veenhuizen, had discussions with Dr. Tuttle sometime around the beginning of 1979 concerning his observations. As a result of those discussions, we initiated a research program directed to evaluating a whole series of  $\beta$ -phenethanolamines as possible growth promoters and leanness enhancers of economic animals such as swine and

ruminants. Our investigations led to the discovery that one compound in particular, namely 31537 (its identifying number within Eli Lilly and Company), has unusually good activity in promoting growth and improving feed efficiency and improving leanness in animals such as ruminants and swine. We have only recently established that one of the four possible optical isomers that comprise 31537, namely 99134, appears to be primarily responsible for the activity exhibited by the 31537 mixture.

Exhibit A, which is attached hereto, is a copy of an internal memo prepared by one J. F. Wagner, an associate working closely at that time with Mr. Veenhuizen at Eli Lilly and Company. The memo reports that discussions had been held with Dr. Tuttle concerning his observation that 99134 caused an increase in lean mass in dogs. The memo further recites that Mr. Veenhuizen had consulted with Drs. Tuttle and Shaw relative to these developments concerning 99134, and that Mr. Veenhuizen intended to explore the possibilities of further work with this class of compounds, namely  $\beta$ -phenethanolamines. Exhibit A further establishes that a meeting of a committee of Eli Lilly and Company referred to as the "Metabolic Control of Growth Committee" was scheduled for January 10, 1979, to further discuss with Dr. Tuttle his work with 99134 and the possibility of evaluating such compound in swine.

Exhibit B is a true copy of the minutes that were taken from the Metabolic Control of Growth Committee meeting that was held on January 10, 1979. The minutes were prepared by Mr. Veenhuizen as Secretary, and establish that discussions were held with Dr. Ron Tuttle in which he reported his observations that 99134 increased the lean mass in dogs. The minutes



indicate that the conclusion was reached that additional study in swine and other economic-type animals would be undertaken with phenethanolamines.

In view of the accompanying documents and the discussions that were held with Dr. Tuttle in early 1979, and in view of the fact that a claim has now been allowed in the above-captioned application directed to the use of 99134 for improving leanness in domesticated animals, we believe Ronald R. Tuttle made an inventive contribution to that claim and should be included as a coinventor in the captioned application.

We further declare that all statements made herein of my own knowledge are true, that all statements made on information and belief are believed to be true, and that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both (18 U.S.C. 1001), and may jeopardize the validity of the application or any patent issuing thereon.

3/11/87  
Date

3/13/87  
Date

3/12/87  
Date

David B. Anderson  
David B. Anderson

Klaus K. Schmieg  
Klaus K. Schmieg

Edward L. Veenhuizen  
Edward L. Veenhuizen

December 22, 1978

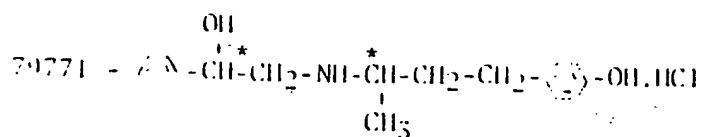
Dr. E. E. Alder  
cc: Dr. J. E. Downing  
Dr. A. L. Melliére  
Dr. A. P. Raun

#### PHENETHANOLAMINES

Dr. Ron Tuttle has observed an increase in lean mass in dogs treated with the phenethanolamine 99134. We have discussed these results with him and have scheduled a committee meeting (Metabolic Control of Growth Committee) for January 10 to discuss further work with this class of compounds in swine.

In 1977 Compound 79771 (also an N-alkylphenethanolamine) was evaluated for lipolytic activity in swine by Dr. Melliére's group. This compound produced a significant increase in plasma free fatty acids, however when given IM daily to pigs abscesses developed at the injection sites and further work was terminated.

Subsequently Compound 99134 was found to be orally active in dogs at relatively low levels (60 mcg/day). The activities measured generally could be described as an increase in lean mass, a decrease in non esterified fatty acids and an increase in heart activity. Mr. Veenhuizen has been in touch with Drs. Tuttle and Shaw relative to these new developments and we intend to explore the possibilities of further work with this class of compounds.



#### PHENETHANOLAMINE

99134 - HO- (3) - (same as 79771)

19134

\*Asymmetric carbon atoms--4 isomers--some with heart contractile and some with lipolytic activity.

J. E. Wagner

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**EXHIBIT A**  
#1 OF 1 PAGES

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METABOLIC CONTROL OF GROWTH COMMITTEE MINUTES (79-1)

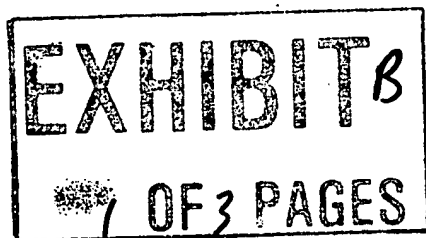
January 10, 1979

Dr. J. F. Wagner, Chairman  
Mr. E. L. Veenhuizen, Secretary  
Dr. J. A. Clemens  
Dr. J. E. Dalidowicz  
Mr. R. G. Edie  
Dr. A. L. Melliere  
Dr. C. C. Scheifinger  
Dr. C. J. Shaar  
Mr. W. A. White

Guests

Dr. R. E. Basson  
Dr. W. N. Shaw  
Dr. E. W. Shuey  
Dr. R. R. Tuttle  
Mr. W. P. Waitt

cc: Dr. E. F. Alder (3)  
Dr. M. E. Amundson  
Dr. R. E. Bowen  
Dr. T. Cebalo  
Dr. J. F. Downing  
Dr. N. R. Easton  
Dr. E. H. Flynn  
Dr. T. M. Folkerts  
Mr. P. D. James  
Mr. W. S. Johnson  
Dr. C. E. Jordan  
Dr. R. W. Kennedy  
Dr. G. F. Kiplinger (Erl Wood)  
Dr. G. C. Klingman  
Dr. R. L. Mann  
Dr. T. M. Mears  
Dr. D. E. Morrison  
Dr. C. F. Murphy  
Mrs. K. R. S. Page  
Dr. A. Pohland  
Dr. G. W. Probst  
Dr. R. P. Rathmacher  
Dr. A. P. Raun  
Dr. R. F. Shumard (Erl Wood)  
Dr. R. F. Sieck  
Dr. Q. F. Soper  
Dr. H. M. Taylor  
Dr. L. V. Tonkinson  
Dr. J. G. Whitney



1. Compound 99134 (a phenethanolamine) - Possible uses in cattle

Dr. Ron Tuttle presented a complete review of the cardiac contractility research using compound 99134 in dogs. In the course of these investigations serum triglycerides and nonesterified fatty acids were reduced within 35 days of treatment. This was similar to the effect of chronic exercise. Additional effects observed indicate an apparent increase in body weight and a reduction in whole body fat. This compound (99134), (R,R)-4-hydroxy-A-[[[3-(4-hydroxyphenyl)-1-methylpropyl]amino]methyl]benzenemethanol, hydrochloride, is highly resolved and is being investigated as an ionotropic agent (heart stimulant) in humans. However, there is a racemic mixture, 31537, which contains about 20% 99134. In addition, there are some analogs which could be tested for their effect on fat metabolism in growing swine. Dr. Shaw reported on his research using compound 104119 in obese rats. This compound is similar but not as cardioactive and is being evaluated as an anti-obesity drug. It appears that there are some side effects with each drug, however, the toxicity levels have been determined and they should not be detrimental to swine.

CONFIDENTIAL

Metabolic Control of Growth

Committee Minutes (79-1)

Page 2

Following considerable discussion concerning the control of fat metabolism in animals the committee agreed that compound 99134 and 31537 should be tested for their effect on growing swine. The initial experiment will be to determine if 99134 is orally active. The drug will be given in the feed and the following physiological measurements will be made:

- 1) Heart rate increase
- 2) Skin temperature increase
- 3) NEFA reduction

Dr. Melliere and Mr. Veenhuizen will develop the protocols. Dr. Scheifinger will work up the electronic systems for monitoring these responses.

Following this initial evaluation a study of longer duration will be conducted to determine the effect on body composition in swine.

EXHIBIT 6  
2 OF 3 PAGES

CONFIDENTIAL

Metabolic Control of Growth  
Committee Minutes (79-1)

Page 3

E. L. Veenhuizen, Secretary  
GL708 811-250

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02-02-79

EXHIBIT 6  
3 OF 3 PAGES



DECLARATION AND POWER OF ATTORNEY

Attorney's Docket No. X-5683B

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APR 10 1987

GROUP 120

As a Below named inventor, I hereby declare that:

My residence, post office address and citizenship are as stated below next to my name.

I believe I am the original, first, and sole inventor (if only one name is listed below) or a joint inventor (if plural names are listed below) of the invention entitled

GROWTH PROMOTION

which is described and claimed in the specification which:

(check ☐ is attached hereto.  
one) ☒ was filed on December 19, 1985  
as Application Serial No. 811,059  
and was amended on (if applicable).

I hereby state that I have reviewed and understand the contents of the above identified specification, including the claims, as amended by any amendment referred to above.

I acknowledge the duty to disclose information which is material to the examination of this application in accordance with Title 37, Code of Federal Regulations, §1.56(a).

Power of Attorney: As a named inventor, I hereby appoint the following attorney(s) and/or agent(s) to prosecute this application and transact all business in the Patent and Trademark Office connected therewith:

Leroy Whitaker, Registration No. 22015, Charles W. Ashbrook, Registration No. 27,610, said Leroy Whitaker to have in addition full power of revocation, including the power to revoke the power herein granted to said Charles W. Ashbrook.

Send Correspondence To:

ELI LILLY AND COMPANY  
Patent Division/CWA  
Lilly Corporate Center  
Indianapolis, Indiana 46285

Direct Telephone Calls To:  
(name and telephone No.)

Charles W. Ashbrook  
(317) 276-6015

DECLARATION AND POWER OF ATTORNEY (cont'd)

Attorney's Docket No. X-5683B

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Full Name of Sole  
or First Inventor : David B. Anderson  
Inventor's Signature : David B. Anderson Date: 3/11/87  
Residence and  
Post Office Address : 1334 Greenhills Road  
Greenfield, Indiana 46140

Citizenship : United States

Full Name of Second  
Joint Inventor, if Any: Klaus K. Schmiegell  
Inventor's Signature : Klaus K. Schmiegell Date: 3/13/87  
Residence and  
Post Office Address : 4507 Staughton Drive  
Indianapolis, Indiana 46226

Citizenship : United States

Full Name of Third  
Joint Inventor, if Any: Edward L. Veenhuizen  
Inventor's Signature : Edward L. Veenhuizen Date: 3/12/87  
Residence and  
Post Office Address : R. R. #3, Box 41  
Greenfield, Indiana 46140

Citizenship : United States

Full Name of Fourth  
Joint Inventor, if Any: Ronald R. Tuttle  
Inventor's Signature : Ronald R. Tuttle Date: 3/19/87  
Residence and  
Post Office Address : 2704 Vista Del Sembrado  
Escondido, CA 92025

Citizenship : United States